

**LISTING OF THE CLAIMS**

**Claim 1 (currently amended)** A method for the production of a single heavy chain antibody in a transgenic non-human mammal comprising the step of expressing a heterologous VHH heavy chain locus in that mammal specifically in B cells in response to antigen challenge, wherein the VHH heavy chain locus is integrated into the non-human mammal's genome and said VHH heavy chain locus comprises:

- (a) at least one VHH exon, at least one D exon and at least one J exon, wherein the VHH exon, the D exon and the J exon are capable of recombining to form VDJ coding sequence, and wherein the VHH exon comprises a naturally occurring VHH coding sequence,
- (b) a constant heavy chain region comprising at least one C $\mu$  constant heavy chain gene and at least one of C $\gamma$ , C $\alpha$ , C $\epsilon$ , or C $\delta$  constant heavy chain gene, wherein each of said constant heavy chain genes, when expressed, does not express a functional CH1 domain,
- (c) a locus control region ("LCR") providing for expression of the VHH heavy chain locus specifically in B cells

said method comprising:

- 1) immunizing said mammal with an antigen and
- 2) isolating single heavy chain antibody against said antigen ~~from said mammal.~~

**Claim 2 (canceled)**

**Claim 3 (canceled)**

**Claims 4 – 6 (canceled)**

**Claim 7 (currently amended)** The method of claim 1 or 41 wherein the VHH single

heavy chain locus comprises a camelid VHH, at least one D exon of human origin and at least one J exon of human origin and a constant region of human origin.

**Claim 8 (canceled)**

**Claim 9 (canceled)**

**Claim 10 (currently amended)** The method of claim 1 or [[3]] 41 wherein the constant heavy chain region comprises at least one constant region heavy chain gene which is of non-camelid origin.

**Claim 11 (original)** A method according to claim 10 wherein at least one constant region heavy chain gene is of human origin.

**Claims 12 – 16 (canceled)**

**Claims 17 -32 (canceled)**

**Claim 33 (currently amended)** The method of claim 1 or 41 wherein the entire VHH single heavy chain locus is of camelid origin

**Claim 34 (previously presented)** The method of claim 3 wherein the camelised VH single heavy chain locus is of human origin.

**Claim 35 (previously presented)** The method of claim 3 wherein the camelised VH single heavy chain locus is of non-human origin.

**Claim 36 (previously presented)** The method of claim 3 wherein the camelised VH single heavy chain locus is of camelid origin.

**Claims 37 -38 (canceled)**

**Claim 39 (currently amended)** The method according to claim 1 or [[3]] 41 wherein the non-human mammal is a rodent.

**Claim 40 (canceled)**

**Claim 41 (currently amended)** A method for the production of a single heavy chain antibody in a transgenic mouse comprising expressing a heterologous VHH heavy chain locus in ~~that mammal said mouse~~ specifically in B cells in response to antigen challenge wherein the VHH heavy chain locus is integrated into the non-human mammal's genome and said VHH heavy chain locus comprises:

(a) at least one VHH exon, at least one-D exon and at least one-J exon, wherein the VHH exon, the D exon and the J exon are capable of recombining to form VDJ coding sequence, and wherein the VHH exon comprises a naturally occurring VHH coding sequence, and

(b) a [[a]] constant heavy chain region comprising at least one C $\mu$  constant heavy chain gene and at least one of C $\gamma$ , C $\alpha$ , C $\varepsilon$ , or C $\delta$  constant heavy chain gene, wherein each of said at least one constant heavy chain gene, when expressed, does not express a functional CH1 domain,

(c) a regulatory sequence providing for expression of the VHH heavy chain locus specifically in B cells

said method comprising:

- 1) immunizing said mammal with an antigen and
- 2) isolating single heavy chain antibody against said antigen ~~from said mammal~~.

**Claim 42 (canceled)**

**Claim 43 (new)** The method of claim 1 or 41 wherein said antibody is isolated using hybridoma technology.

**Claim 44 (new)** The method of claim 1 or 41 wherein said antibody comprises a variable region fragment and said variable region fragment is isolated using phage display.